



Urban climate modified short-term association of air pollution with pneumonia mortality in Hong Kong

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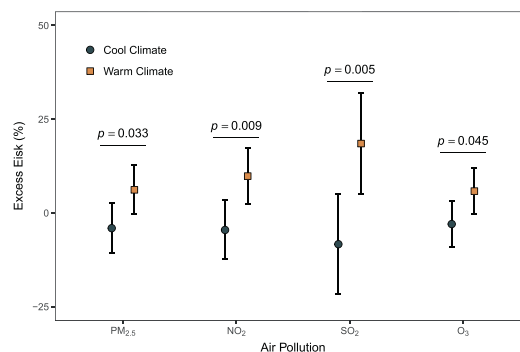
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HIGHLIGHTS

- Whether warmer climates intensify air pollution-pneumonia mortality is unknown.
- We used urban climatic map to define urban climate.
- Warmer climates worsened association of pneumonia mortality with air pollution in Hong Kong.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: City is becoming warmer, especially in the process of urbanization and climate change. However, it is largely unknown whether this warming urban climate may modify the short-term effects of air pollution.

Objectives: To test whether warmer urban climates intensify the acute mortality effects of air pollution on pneumonia in Hong Kong.

Methods: Participants who died of pneumonia from a prospective Chinese elderly cohort between 1998 and 2011 were selected as cases. Urban climatic (UC) classes of cases were determined by an established Urban Climatic Map according to their residential addresses. UC classes were first dichotomized into cool and warm climates and case-crossover analysis was used to estimate the short-term association of pneumonia mortality with air pollution. We further classified UC classes into climate quartiles and used case-only analysis to test the trend of urban climate modification on the short-term association of pneumonia mortality with air pollution.

Results: Among 66,820 elders (≥65 years), 2208 pneumonia deaths (cases) were identified during the 11–14 years of follow-up. The effects of air pollution for cases residing in the warm climate were statistically significant ($p < 0.05$) higher than those living in the cool climate. There was an increasing linear trend of urban climate modification on the association of pneumonia mortality with NO₂ (nitrogen dioxide) (p for trend = 0.035). Compared to climate Quartile 1 (the lowest), deaths resided in climate Quartile 2, 3, and 4 (the highest) were

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associated with an additional percent change of 9.07% (0.52%, 17.62%), 12.89% (4.34%, 21.43%), and 8.45% (–0.10%, 17.00%), respectively.

Conclusions: Warmer urban climate worsened the acute mortality effects of pneumonia associated with air pollutants in Hong Kong. Our findings suggest that warmer urban climate introduced by climate change and urbanization may increase the risks of air pollution-related pneumonia.

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1. Introduction

Pneumonia is one of the most common infectious diseases and is a leading cause of morbidity and mortality worldwide (World Health Organization, 2008). It affects about 450 million people globally and results in approximately 4 million deaths per year, accounting for 7% of the world's total deaths (Ruuskanen et al., 2011). The annual incidence of pneumonia in the elder population is up to four-times than that of the younger group (Janssens and Krause, 2004). With the world is aging rapidly, pneumonia is becoming a major global public health problem.

Air pollution is recognized as the world's largest single environmental problem (Landrigan et al., 2018), and it is one significant risk factor for pneumonia diseases, especially for elders (Zanobetti and Woodhead, 2010). The adverse effects of air pollution on pneumonia morbidity and mortality have been well documented (Faustini et al., 2013; Meng et al., 2012; Nhung et al., 2018; Tian and Sun, 2017). However, the relative risk magnitudes of air pollution effects differ according to geographical regions (Katsouyanni et al., 2009; Kioumourtoglou et al., 2015). For instance, a large-scale multi-city epidemiological study (Katsouyanni et al., 2009) reported that relative risk estimates for both particulate matter and ozone (O₃) showed substantial heterogeneities among cities in Canada, Europe, and the United States. One of the proposed factors to explain the observed effect heterogeneity of air pollution was the city climate. However, no study has tested this hypothesis by utilizing a reliable tool to characterize the city climate.

With climate change and urbanization, urban is warming rapidly. Pneumonia is a climate-sensitive disease (Sun et al., 2018). It is warranted to test whether this warming climate intensifies the short-term association between air pollution and pneumonia. Although numerous studies reported that temperature (short-term) modified the health effects of air pollution, unlike temperature, people may acclimate to local climate (long-term). In the present study, we aimed to investigate the modification effects of urban climate on the short-term association of air pollution with pneumonia mortality among elders in Hong Kong from 1998 to 2011. We hypothesized that warmer urban climate might increase the risk of pneumonia mortality with air pollution.

2. Methods

2.1. Study population

This study leveraged on a prospective Chinese elderly cohort with a total population of 66,820 older people (65+ years), about 9% of Hong Kong elders, who enrolled at one of the 18 Elderly Health Centres from 1998 to 2001, and were followed up till 31 December 2011 (Schooling et al., 2014). Details of this cohort profile have been described (Schooling et al., 2014). The cohort was linked with the death registration in the Department of Health using the Hong Kong identity card number. We identified pneumonia death by using codes of International Classification of Diseases, 9th revision (ICD-9): 480–487 or ICD-10: J10–J18. Ethics approval was approved by the Ethics Committee of the Faculty of Medicine, The University of Hong Kong and the Hong Kong Department of Health.

2.2. Air pollution and meteorological data

We obtained daily 24-h average concentrations of particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}), nitrogen dioxide (NO₂), sulphur dioxide (SO₂), and ozone (O₃) from ten general monitoring stations from 1998 to 2011 in Hong Kong (Fig. 1). Daily air pollution concentrations were calculated by taking average of the daily air pollution concentrations across the ten monitoring stations. We extracted daily mean ambient temperature and relative humidity for the same study period from the Hong Kong Observatory. The influenza epidemic was defined as a weekly number of positive influenzas A + B isolates $\geq 4\%$ of the annual total number of positive isolates for at least two consecutive weeks (Chiu et al., 2002; Thach et al., 2010).

2.3. Urban climatic map

Urban Climatic Map (UCMap) constitutes a holistic approach towards understanding the outdoor microclimate conditions. It adequately displays the spatial characteristics and classification of climatopes representing areas of distinct local climates (Planning Department, 2012). Over fifteen countries have developed UCMaps to guide their urban planning (Ren et al., 2011). The methodology of developing the Hong Kong UCMap was described elsewhere (Planning Department, 2012). Briefly, it collated six layers of information, including building volume, topographical height, ground coverage, natural landscape, proximity to openness, and green space. It used Physiologically Equivalent Temperature (PET) (Höppe, 1999), a thermal index and a synergetic indication of human thermal comfort, to calibrate the classification of microclimates. The developed UCMap was verified and calibrated by field measurement and thermal comfort survey study (Planning Department, 2012). Hong Kong was classified into fourteen climatic (UC) classes (Fig. 2). Assuming a mobile radius of 500 m (Requia et al., 2016), we estimated the UC class of each pneumonia death (case) by calculating the area-weighted average of UC classes within 500 m buffer of the case's residential address. Pneumonia cases were then dichotomized into those resided in cool and warm urban climates based on the median (UC class = 0.74) of the UC classes of cases. To investigate the trend of urban climate modification on the association between air pollution and pneumonia mortality, we further divided pneumonia deaths into quartiles according to their UC classes: Quartile 1 (UC classes ranging from –4.10 to –1.59), Quartile 2 (–1.59 to –0.74), Quartile 3 (–0.74 to 0.08), and Quartile 4 (0.08 to 2.70) (Fig. S1).

2.4. Statistical analysis

Time-stratified case-crossover study design was used to estimate the association of air pollution with pneumonia mortality, which is one of the most widely used study designs to investigate the acute health effects of air pollution (Carracedo-Martinez et al., 2010; Jaakkola, 2003). The concept of this approach is similar to a case-control study, except that now cases and controls are the same subject but in different times (Janes et al., 2005; Levy et al., 2001). Each case serves as his/her own control, thus personal characteristics have been controlled by this study design. For each death, the case day is the day of death and the control days are the same weekdays within the same month and year of death (Carracedo-Martinez et al., 2010). Because of

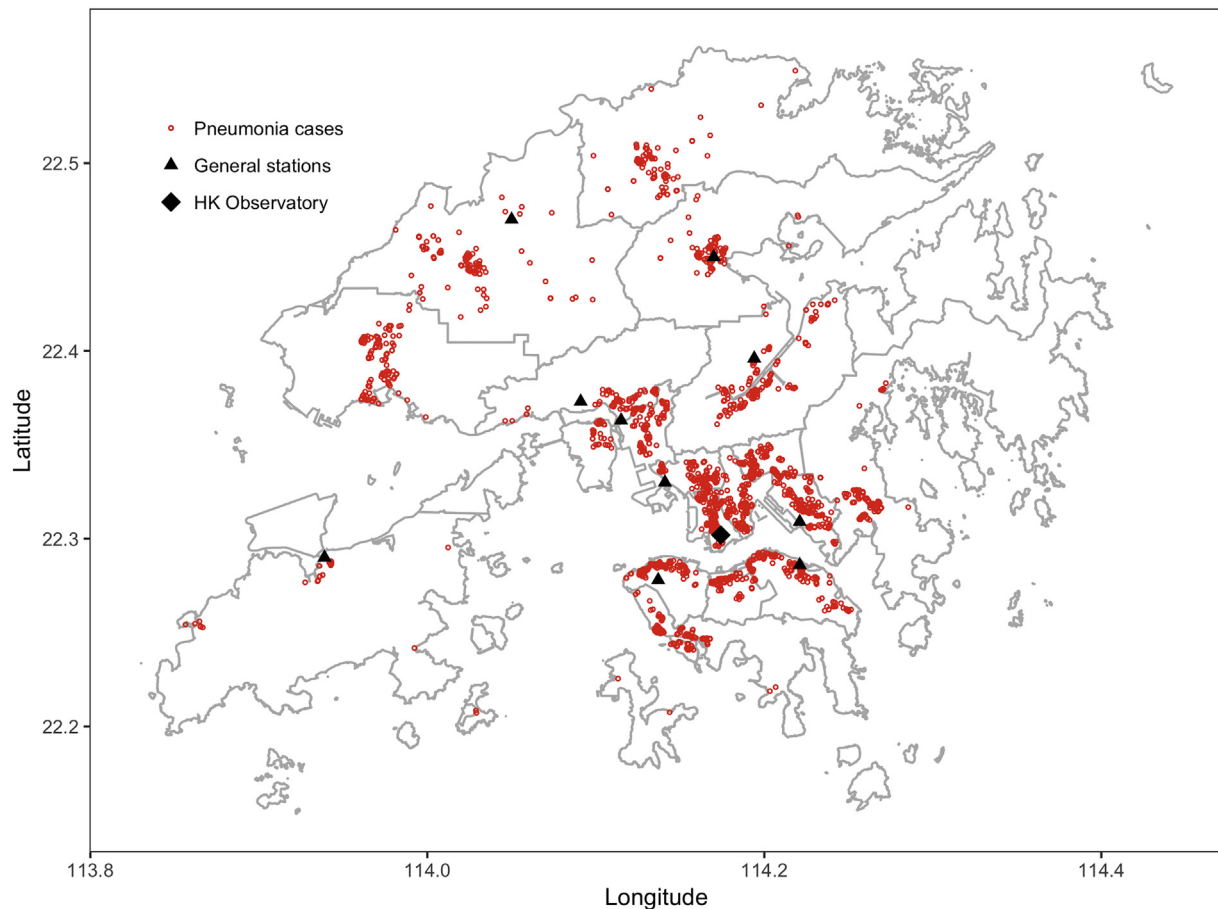


Fig. 1. Spatial distribution of pneumonia cases ($n = 2208$), general air monitoring stations ($n = 10$) and the Hong Kong Observatory.

such matching, long-term and seasonal trends and time-fixed confounders have been well controlled. We further controlled for time-varying confounders including ambient temperature, relative humidity, and influenza epidemics. To control for the nonlinear and delayed effects of temperature, we created a cross-basis term of temperature using a natural cubic spline (NCS) with four knots placed at equal space in the temperature range and a NCS with three knots placed at equal intervals on the lag scale of lags up to 21 days before death (Buteau et al., 2018; Sun et al., 2016). We also controlled for relative humidity (rh) by including a NCS with three degrees of freedom (df). Our model is shown as follows:

$$\text{Logit}[P(Y)] = \text{Strata}(\text{strata}) + \beta_1 AP + \beta_2 \text{Influenza} + \text{Temp}_{t,l} + ns(rh, df = 3)$$

where *Strata* (*strata*) represents risk set, *AP* is air pollution; β_1 is the estimated coefficient for air pollution; *Influenza* is a binary variable for influenza epidemic, $\text{Temp}_{t,l}$ is the created cross-basis term to model effects of temperature, and $ns(\cdot)$ denotes a natural cubic spline function.

Because the incubation period of viral and bacterial infections may be as long as a week (Lessler et al., 2009; Winchell, 2013), we calculated mean values of air pollution 6 days prior to the day of the event [denoted as the weakly moving average (lag_{0-6})]. We conducted stratified analysis by cool and warm urban climate. We tested the differences between risk estimates of air pollution in cool and warm urban climate by $(\widehat{Q}_1 - \widehat{Q}_2) / \sqrt{(\widehat{SE}_1)^2 + (\widehat{SE}_2)^2}$, where $\widehat{Q}_1$ and $\widehat{Q}_2$ are the risk estimates for the cool and warm urban climates, and $\widehat{SE}_1$ and $\widehat{SE}_2$ are their respective standard errors (Altman and Bland, 2003; Zeka et al., 2006). The flow chart of the case-crossover data analysis was summarized in Fig. S2.

To assess the trend of urban climate modification, we further categorized pneumonia cases into those resided in climate Quartile 1 (the lowest), Quartile 2, Quartile 3, and Quartile 4 (the highest), respectively. We used case-only analysis to evaluate the trend of the modification effects of urban climate on the association of pneumonia mortality with air pollution. This approach has been widely used to identify subpopulation who is more susceptible to air pollution (Medina-Ramon and Schwartz, 2008; Wong et al., 2008). Compared to the “conventional” regression analyses (e.g., time-series or nested case-control study), case-only analysis reduces the vulnerability to model misspecification bias and has slightly more study power on accessing the modification (Armstrong, 2003; Zanobetti et al., 2013). A detailed description of this approach has been published (Armstrong, 2003; Schwartz, 2005).

The underlying idea of case-only analysis in the present study is that people who died of pneumonia on high concentration of air pollution days would be prone to reside in warmer urban climates than those who died on low-level air pollution days, and hence the concentrations of air pollution at the date of death could be a predictor of urban climate quartiles of the pneumonia cases. We treated urban climate quartiles (potential modifier) as the dependent variable and air pollution concentrations as the predictor. Multinomial logistic regression was used to estimate the additional change of pneumonia mortality in warmer urban climate quartiles (Quartile 2 to Quartile 4) compared to climate Quartile 1 (reference). Ordinal logit model was used to evaluate whether there was a linear trend in the risk estimates of air pollution on pneumonia mortality across increasing climate quartiles. The flow diagram of the case-only analysis was summarized in Fig. S3.

A number of sensitivity analyses have been conducted to check the robustness of our findings: (1) we used 800 m buffer to assign pneumonia deaths' urban climatic classes; (2) to rule out the possibility of

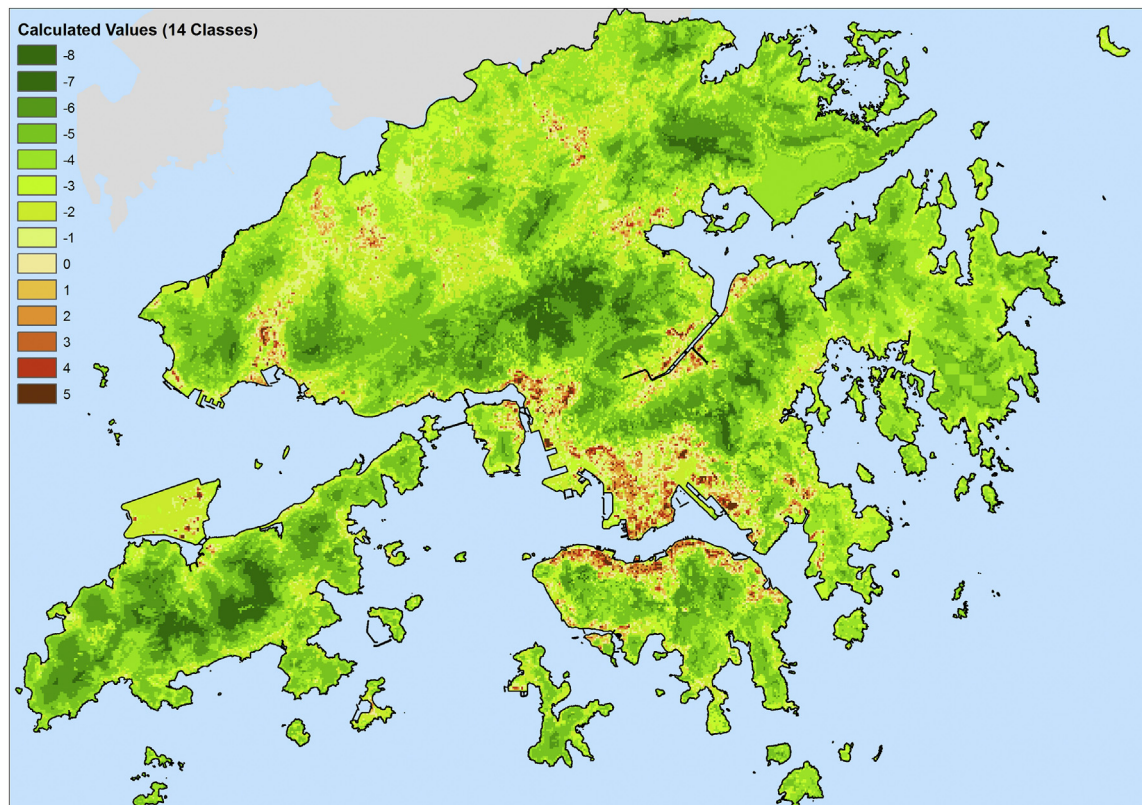


Fig. 2. The Hong Kong Urban Climatic Map in 2000 at a grid resolution of 100 m × 100 m. The diversity of microclimate in the whole territory is classified into fourteen urban climatic classes with a range from −8 to 5. The higher the urban climatic class, the warmer the microclimate.

confounding from ambient temperature and long-term and seasonal trends, we further controlled for the seasonal pattern using a sine and cosine term with a 365.24-day period and ambient temperature at lag₀ in the case-only study; and (3) to control neighborhood-level confounding, we conducted a nested case-control study (“traditional” regression analysis) after controlled for all measured confounders that included individual-level confounders (age, sex, alcohol consumption, physical activity, smoking status, body mass index, education attainment, medication taken, personal monthly expenses, and baseline annual concentration of PM_{2.5} to represent long-term air pollution exposure), tertiary planning unit-level confounders (proportion of people aged 65 years or older, proportion of people with tertiary education, and proportion of people with monthly domestic household income ≥1923 USD), and district-level proportion of smoker, in addition to time-varying confounders (day of the week, ambient temperature, relative humidity, and influenza epidemics) (Supplementary material).

All analyses were conducted in R3.4.2 with ‘survival’, ‘nnet’, ‘ordinal’, and ‘dlnm’ packages.

3. Results

The diversity of urban microclimates in Hong Kong was classified into fourteen UC classes ranging from −8 to 5 (Fig. 2). A higher UC class number indicates an area with a warmer urban microclimate. These fourteen UC classes were further categorized into eight classifications (Table 1). We identified 2208 cases who died of pneumonia during the 11–14 years of follow-up from 1998 to 2011 (Fig. 1). Based on UCMAP, we calculated the weighted UC class for each case according to his/her residence address. The UC classes of pneumonia cases were ranging from −4.1 to 2.7. We used the median (−0.74) of UC classes to divide pneumonia deaths into those resided in cool and warm urban climate or used quartiles of UC classes of pneumonia cases to

divide pneumonia deaths into four categories with corresponding cut-off points of UC class at −1.59, −0.74, and 0.08, respectively (Fig. S1).

The time-series plots of daily concentrations of air pollution were shown in Fig. 3. The daily mean concentration (standard deviation) was 35.4 µg/m³ (20.6 µg/m³), 53.2 µg/m³ (18.8 µg/m³), 17.8 µg/m³ (11.8 µg/m³), and 36.8 µg/m³ (20.3 µg/m³) for PM_{2.5}, NO₂, SO₂, and O₃, respectively.

The risk estimates of air pollution on pneumonia mortality were stronger in the warm climate than the cool one (Table 2). For example, the percent excess risk (ER%) per 10 µg/m³ increase in the weekly moving average exposure (lag_{0–6}) of PM_{2.5} was −4.06% (−10.77%, 2.64%) and 6.17% (−0.39%, 12.74%) in the cool and warm climate, respectively. The difference between ER% of air pollution in the cool and warm climate was statistically significant ($p < 0.05$).

Table 3 shows the additional percent change in pneumonia mortality associated with air pollution by urban climate quartiles. We observed an increasing trend in the risk estimates of NO₂ from climate Quartile 1 to Quartile 4 (p for trend = 0.035). When compared to

Table 1

The correspondence of urban climatic (UC) classes with the approximate physiologically equivalent temperature (PET) differences and their impacts on thermal comfort.

UC class	Classification	Approximate PET difference	Impact on thermal comfort
−8, −7, −6	1	−2	Moderate cooling
−5, −4	2	−1	Slight cooling
−3, −2	3	0	Neutral
−1	4	+1	Slight warming
0	5	+2	Moderate warming
1	6	+3	Moderately strong warming
2, 3	7	+4	Strong warming
4, 5	8	+5	Very strong warming

The PET interval between each classification is in the order of about 1 °C. For example, PET in class 5 is approximate 2 °C higher than that in class 3.

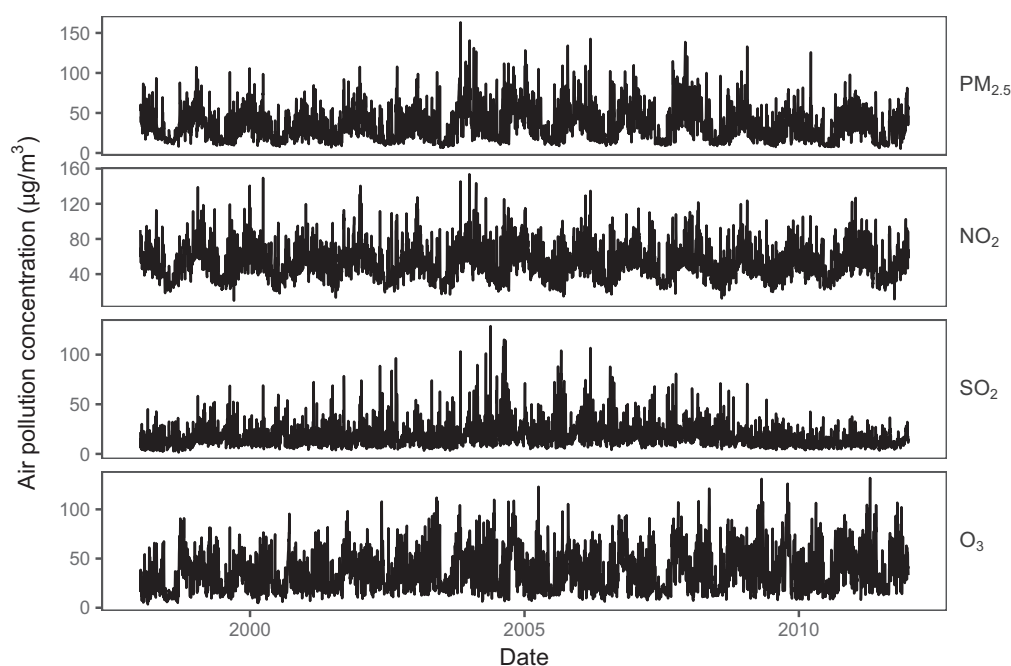


Fig. 3. Time-series plots of daily mean air pollutants.

climate Quartile 1, the additional percent change in pneumonia mortality for NO_2 increased $10 \mu\text{g}/\text{m}^3$ at lag_{0-6} in climate Quartile 2, Quartile 3, and Quartile 4 was 9.07% (0.52%, 17.62%), 12.89% (4.34%, 21.43%), and 8.45% (−0.10%, 17.00%), respectively. However, we did not observe an increasing trend for $\text{PM}_{2.5}$, SO_2 , and O_3 . Our study findings did not change substantially when we used 800 m buffer to assign climatic classes to participants or further controlled for ambient temperature and seasonality pattern in the case-only study (Table S1 and Table S2). Results of the nested case-control study also confirmed the robustness of our findings (Table S3).

4. Discussion

In the present study, pneumonia cases resided in the warm climate or warmer climate quartiles were associated with stronger acute mortality effects of air pollution on pneumonia, especially for NO_2 air pollution. Our findings indicate that warmer urban climate may worsen the association of pneumonia mortality with air pollution.

Our findings were consistent with a few large-scale multicity studies using annual mean temperature or using latitude to represent city climate which suggested that the risk estimates of air pollution were higher in warmer cities (Katsouyanni et al., 2009; Katsouyanni et al., 2001; Kioumourtoglou et al., 2015). For example, the Air Pollution

and Health: A European Approach Phase-2, a large-scale multi-city epidemiological study, examined 29 European cities, and reported that mortality effect of PM_{10} per $10 \mu\text{g}/\text{m}^3$ increase in ER% was stronger in cities with warm climate (0.82%) than that in relatively cold climate (0.29%) (Katsouyanni et al., 2001).

Although few studies have investigated the interaction between climate and air pollution on human health, a great number of epidemiological studies have investigated the modification effects of weather (De Sario et al., 2013; Medina-Ramon et al., 2006; Meng et al., 2012; Sun et al., 2015). Meng et al. (2012) examined eight Chinese cities with a total population of 36.1 million and demonstrated that the risk estimates on high temperature days (>95th percentile) versus normal temperature days (5th–95th percentile) increased by 0.81% for total mortality, 1.01% for cardiovascular mortality, and 0.99% for respiratory diseases per $10 \mu\text{g}/\text{m}^3$ increment in PM_{10} . These findings were based on the short-term modification of weather, instead of urban climate modification where we need to take potential acclimatization into account.

The human lung has an exquisite and complex defense against invading microbes, the first line of which is airway epithelial cells. Airway epithelial cells are primarily through activating alveolar macrophages to clear invading microbes when they sense a rise in bacterial products (Camberlein et al., 2015; Eddens and Kolls, 2012). However, when the epithelial barrier is penetrated by microbes, pneumonia could rapidly develop.

The underlying mechanisms of the adverse health effects of air pollution on pneumonia mortality intensified by warmer urban climate are not clear yet. It is possible that human body responses to warmer climate may increase the total intake of airborne pollutants by activating three key systems to dissipate excess heat: cardiovascular, respiratory, and sudomotor (Gordon, 2003). Air pollutants were reported to impair the function of alveolar macrophages and epithelial cells, which would increase respiratory epithelial permeability, thereby might increase the risk of lung infections (Chauhan and Johnston, 2003; Frampton et al., 1989; Kehrl et al., 1987; Zhou and Kobzik, 2007). The additional air pollution intake in the warmer climate might further reduce the lung macrophage antibacterial function and increase the permeability of respiratory epithelium for virus and bacterial pathogens, which

Table 2

Percent excess risk (ER%) and 95% confidence interval of pneumonia mortality per $10 \mu\text{g}/\text{m}^3$ increase in the weekly moving average of air pollutants in the cool and warm climate, respectively^a.

Air pollutant	Cool climate	Warm climate	p-Value
$\text{PM}_{2.5}$	−4.06 (−10.77, 2.64)	6.17 (−0.39, 12.74)	0.033
NO_2	−4.53 (−12.40, 3.34)	9.83 (2.36, 17.29)	0.009
SO_2	−8.33 (−21.71, 5.05)	18.51 (5.12, 31.90)	0.005
O_3	−2.96 (−9.09, 3.18)	5.83 (−0.21, 11.86)	0.045

Abbreviations: $\text{PM}_{2.5}$ = particulate matter $\leq 2.5 \mu\text{m}$ in aerodynamic diameter; NO_2 = nitrogen dioxide; SO_2 = sulphur dioxide; O_3 = ozone.

^a Cool and warm urban climate were defined by the medium of urban climatic classes of the pneumonia cases.

Table 3

Additional percent changes and 95% confidence interval in pneumonia mortality associated with 10 $\mu\text{g}/\text{m}^3$ increase at the weekly moving average (lag_{0-6}) of air pollutants by urban climate quartiles^a.

Air pollutant	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p for trend ^b
PM _{2.5}	Reference	5.66 (−1.64, 12.96)	6.65 (−0.63, 13.94)	5.86 (−1.43, 13.16)	0.117
NO ₂	Reference	9.07 (0.52, 17.62)	12.89 (4.34, 21.43)	8.45 (−0.10, 17.00)	0.035^c
SO ₂	Reference	12.82 (−4.26, 29.90)	22.27 (5.47, 39.06)	9.09 (−8.11, 26.29)	0.192
O ₃	Reference	2.81 (−4.81, 10.44)	3.07 (−4.55, 10.69)	4.72 (−2.88, 12.32)	0.237

Abbreviations: PM_{2.5} = particulate matter $\leq 2.5 \mu\text{m}$ in aerodynamic diameter; NO₂ = nitrogen dioxide; O₃ = ozone.

^a Climate quartiles were based on quartiles of UC classes of cases. The additional percent changes (and 95% CI) were generated from multinomial logistic regression models.

^b p for trend was estimated by fitting ordinal logit model to determine whether there was a linear trend in the health effects of air pollution increasing from urban climate Q₁ (the lowest) to Q₄ (the highest).

^c Statistically significant.

might accelerate the development of pneumonia. Also, warming climate may influence viral activity and transmission (e.g. respiratory syncytial virus) (Donaldson, 2006; Mirsaiedi et al., 2016), alter vectors and the host immune response (D'Amato et al., 2015; Dobson, 2009), which may increase the mortality effects of air pollution. Finally, the larger impact of air pollution in warmer climate may relate to unmeasured factors that correlate with urban climate, such as the accessibility to medical care. Although we controlled for measured potential confounders that included personal characteristics and neighborhood factors (tertiary planning units- and district-level confounders) in the nested case-control study, residual or unmeasured confounding was still possible.

Our study has some strengths. First, to our knowledge, our study was the first to test the hypothesis that urban climate might modify the mortality effects of air pollution on pneumonia via utilizing a reliable tool to display the spatial characteristics and classification of urban climate. Second, the study site, Hong Kong, is highly-urbanized and is one of the most populated cities in the world. Hong Kong has one of the highest within-territory spatial difference in surface temperature ($\sim 8^\circ\text{C}$ in range) compared to other cities in the world (Memon et al., 2009). The perquisites of high within-territory spatial difference in surface temperature and the availability of the UCMAP enable us to test this hypothesis.

Some limitations need to be acknowledged. First, the study participants were the deaths from a specific population, a prospective Chinese elderly cohort in Hong Kong, thus the generalizability of the findings in this study needs to be further tested in other populations and locations (Schooling et al., 2014). Second, UCMAP was developed based on the meteorological conditions of summer months, misclassification error for climate assignment might exist. However, urban is warmer than rural areas even in winter (Giridharan and Kolokotroni, 2009), thus this misclassification would not bias our findings significantly. Finally, we used average concentrations from ten fixed-site air monitoring stations as a proxy for each participant's exposure, which may introduce potential measurement errors. However, the daily air pollution concentrations among the ten air monitoring stations were highly correlated (Fig. S4–Fig. S7), and thus the potential bias due to exposure misclassification should be negligible.

Our findings have some significant implications. With climate change and urbanization, cities are becoming warmer, especially megacities. Our study highlights the potential impacts of climate change and urbanization on the association between air pollution and pneumonia mortality. Our findings imply that urban planning designed to improve climatic conditions or taking climate change mitigation actions may reduce the adverse health effects of air pollution which may bring additional health benefits. This may be another incentive for governments to take climate change mitigation actions earlier.

In conclusion, elders residing in warmer urban climates had stronger mortality effects of air pollution on pneumonia in Hong Kong. This finding highlights that warmer climate introduced by climate change and urbanization may intensify the adverse health effects of air pollution on pneumonia.

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Declaration of interests

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2018.07.311>.

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